the nature of the procedure precludes identification of specific cell types under observation.

Nevertheless, the use of cytotoxic tests is becoming increasingly more popular, and is promoted in nonprofessional books and magazines,[8] particularly those that encourage self-help in matters of health and well-being. Newspaper advertisements throughout California appear regularly from laboratories offering this test directly to the public without the requirement that patients be seen by a physician. One such advertisement in a gay newspaper implied that the cytotoxic test for food allergy can be used in the diagnosis of acquired immune deficiency syndrome (AIDS).

In California an unlicensed laboratory can offer the test directly to the public because of a determination by the Laboratory Field Services division of the Department of Health Services that "information derived from cytotoxic testing is not used to diagnose 'disease in human beings' " (as defined by the Business and Professions Code) "but rather is being used to provide dietary counseling" (R. D. Hamblin, written communication, April 1982).

This ruling is a clear denial of the obvious facts. The originator and proponents of the test devised it for the specific purpose of establishing the diagnosis of food allergy. The test is usually offered for the determination of "allergy" to 150 or more foods at a cost to the patient of $300 to $500. The patient receives a copy of the "results" and an explanation stating (1) that this is a "test," (2) that a positive result indicates that certain foods are toxic to the patient's leukocytes and (3) that the patient is therefore allergic to that food.

The problem of allergy to foods is a controversial one that divides allergists and confuses physicians and patients alike. Anaphylactic reactions to foods, especially seafoods, legumes, nuts and berries, are well recognized, easily diagnosed and fortunately rare. Delayed gastrointestinal reactions to foods are more common and probably encompass both allergic and nonallergic causes. The association of other adverse effects with foods, particularly behavioral and cognitive changes and poorly defined symptoms such as fatigue, are in most cases spurious, as shown by double-blind challenge studies of May[9] and others. Certain foods contain pharmacologically active chemicals, occurring either naturally or by contamination or deliberate addition, and these may be responsible for adverse effects in some patients. A thorough clinical history is essential in the evaluation of each case.

A practitioner who is confronted by a difficult diagnostic problem may be tempted to order a cytotoxic test. Before doing so, the physician must be aware that the test procedure—while appearing to be a diagnostic test—has no rational basis or proved ability to detect allergy or to determine the nutritive value of foods. An elimination diet based on a faulty test is not in a patient's best interest and can reinforce the belief in a nonexistent food allergy in addition to risking the development of nutritional difficulties.

California's Department of Health Services is wrong in its interpretation of the cytotoxic test. The test cannot offer information useful in dietary counseling, and it cannot be used to diagnose allergy. Nevertheless it is *in fact* being used for this purpose, and laboratories offering the test are diagnosing disease and therefore engaging in the practice of medicine. Permitting unlicensed laboratories to carry out a worthless and misleading procedure is a clear abrogation of the role of government in protecting the public's health through its regulation of health facilities.

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REFERENCES

1. Black AP: A new diagnostic method in allergic disease. Pediatrics 1956; 17:716-721
2. Vaughan WT: The leucopenic index as a diagnostic method in the study of food allergy. J Lab Clin Med 1936; 21:1278-1288
3. Bryan WTK, Bryan MP: The application of in vitro cytotoxic reactions to clinical diagnosis of food allergy. Laryngoscope 1967; 70: 810-815
4. Bryan WTK, Bryan MP: Cytotoxic reactions in the diagnosis of food allergy. Otolaryngol Clin North Am 1971; 4:523-534
5. Golbert RE: A review of controversial diagnostic and therapeutic techniques employed in allergy. J Allergy Clin Immunol 1975; 56:170-190
6. Grieco MH: Controversial practices in allergy. JAMA 1982; 247: 3106-3111
7. Rose NR, Friedman H: Manual of Clinical Immunology, 2nd Ed. Washington, DC, American Society for Microbiology, 1980
8. Prokap D: A super diet for athletes. Runner's World 1981; 16:58-63
9. May CD, Bock SA: A modern clinical approach to food hypersensitivity. Allergy 1978; 33:166-188

Prolactinoma

IN THIS ISSUE Dr Martin and colleagues have reviewed their experiences and impressions regarding the epidemiology, presentation, diagnosis and treatment of prolactinoma—the most common hypothalamic-pituitary disease seen in clinical practice.[1] Why is the disease so common and has its incidence changed? We have no evidence that the disease is occurring any more frequently now than previously. The diagnosis was clearly missed before prolactin was recognized in 1971 as a hormone separate and distinct from the growth hormone in humans. With the advent of specific and sensitive radioimmunoassays for prolactin, hyperprolactinemia was demonstrated to be a common condition that accounted for not only 15% to 30% of cases of amenorrhea in gynecologic practice, but also for 50% to 60% of cases of the hitherto most common pituitary tumor—the "nonfunctioning" tumor.[2]

All endocrine tissues have a propensity for adenoma formation and the pituitary is no exception. The study by Costello indicates that this is certainly true.[3] As it was carried out in the 1930s, this study did not address whether those tumors were prolactinomas. More recently, however, Burrow and co-workers evaluated postmortem radiographic and macroscopic and microscopic findings in the pituitary and showed there was a significant incidence (11%) of prolactinoma in both men and women at all ages.[4] Furthermore, they provided data that questioned the specificity of tomography in identifying changes of the sella turcica associ-

ated with microadenomas. What, then, is the optimum neuroradiological approach for examination of the pituitary in 1983? Most investigators agree that neither plain skull x-ray films nor tomography is helpful in diagnosing microadenomas or, for that matter, macroadenomas. These radiological techniques examine the bony tissues rather than the soft tissues of the pituitary. The high-resolution computed tomography (CT) scan best defines the pituitary anatomy (including soft tissue) and allows diagnosis of macroadenomas and some microadenomas, as well as identification of suprasellar extension or empty sella syndrome. Indeed, the need for pneumoencephalography for pituitary disease is now almost entirely eliminated.

Who should be screened for the presence of a prolactinoma and are there any pathognomonic signs of the condition? The incidence and presentation of a prolactin-secreting adenoma are different in men and women, although the pathological studies would suggest the prevalence of prolactinomas is similar in the two sexes.[4] The condition is more frequently diagnosed in women who present with menstrual problems or infertility. Although women often have galactorrhea, some do not, even on careful examination. Because about 50% of women with galactorrhea have normal serum prolactin levels, the presence of galactorrhea is a poor discriminator of the presence or absence of hyperprolactinemia. Examination of the large surgical series of 330 patients reported by Hardy shows that 68% of the women had microadenomas, while 83% of the men had macroadenomas.[5] Thus the men present late in the course of their disease with symptoms resulting from expansion of their tumor, such as visual field defects and headaches. They too are hypogonadal but are often unaware of this until following treatment they realize all they have been missing!

The major controversy in this subject relates to the optimal management of these patients. At the outset it has to be stated that there are certain unknowns which make it impossible to give a definitive answer. Such questions include the following: (1) What is the natural history of a prolactinoma? (2) What are the surgical results? (3) How often is recurrence seen after a "successful" surgical procedure? (4) Does medical therapy affect the natural history of the disease? The answers to each question are long, circuitous and unsatisfactory. It is likely that in most instances these tumors run a very benign course and probably do not progress; occasional tumors, however, are aggressive and the question is how to distinguish them prospectively; at present there is no answer.

The surgical results vary. The perspective given in Dr Martin's paper is biased because the University of California, San Francisco (UCSF), is a major national referral center for pituitary microsurgery and their results are not representative of neurosurgical removal of microadenomas in an average hospital. Even in the major centers such as UCSF, where operations are carried out every day by highly skilled neurosurgeons specializing in transsphenoidal pituitary microsurgery, the results are only satisfactory when the pretreatment serum prolactin value is less than 200 ng per ml. Moreover, a definite incidence of recurrence of hyperprolactinemia months or years later is now being recognized[6] and, therefore, the simplistic view of the operation as a lifelong cure has to be questioned.

What about medical therapy? Medical therapy with dopamine-agonist drugs, of which bromocriptine is the prototype, is well established and experience now spans 13 years in Europe. Bromocriptine has been approved for limited application in the United States. The drug, acting as a functional analogue of dopamine, the physiological prolactin-inhibiting hormone, is able to lower prolactin levels and restore gonadal function in more than 90% of patients with hyperprolactinemia who have not undergone a previous operation or irradiation. The effect of the therapy, however, persists only for the duration of treatment. This limitation is not itself a rationale for rejecting medical treatment, as it may be viewed as replacement therapy. By analogy we consider lifelong thyroxine therapy very satisfactory for treating hypothyroidism. Not only are prolactin levels lowered by bromocriptine but the vast majority of these tumors become smaller in days or weeks.[7,8] The effect again persists for only as long as therapy is continued, and the tumors usually increase in size when treatment is withdrawn.[9,10] The dilemma, therefore, has reversed itself. Originally it was argued that small tumors produced no compressive symptoms and, therefore, could be treated medically, while large tumors required surgical decompression even if they could not be cured. Now we realize that only the small tumors can be cured by surgical resection and medical and surgical results (from the major centers only) are comparable. The large tumors are often difficult to resect and postoperatively patients often suffer permanent pituitary deficiencies in addition to persistent hyperprolactinemia. Therefore, surgeons are now pretreating their patients with bromocriptine in the hope of shrinking the tumors to make them more surgically accessible. The hope is that this would improve the cure rate in the larger tumors. As yet no series of any size has been published to demonstrate whether or not this assumption is correct. I believe it is unlikely, since the large prolactinomas associated with the highest prolactin levels are usually invasive and shrinkage of the tumors may not allow any better clearance of cells that have invaded either the periosteum, dura or cavernous sinus. On the other hand, if the tumor is shrunken into the fossa, the tumor may be decompressed more easily; thus the morbidity of the operation and the incidence of hypopituitarism may be reduced.

The question "why operate?" has to be asked when a tumor is shrunken, compressive symptoms have resolved, prolactin levels lowered and gonadal function restored with bromocriptine. One answer would be that once treatment is stopped the condition will recur. In itself this is true but in my view is not justification for a surgical procedure. If a patient chooses not to take lifelong dopamine-agonist therapy, then surgical

treatment is clearly indicated. However, if a patient understands that she or he will need to undergo lifelong medical therapy, then in my view medical therapy alone is a reasonable approach. Others have suggested that these patients should undergo external pituitary irradiation after the tumor has been treated with medical therapy. In this way medical therapy may be stopped after several years and the condition may not recur. This is speculation, however, and has yet to be proved. Additionally, the risk of development of hypopituitarism must be considered.

What about asymptomatic patients who are amenorrheic and have mild hyperprolactinemia; should they be treated? Such patients should at least be offered a short (six months) course of medical therapy. When they are euprolactinemic they often recognize an increase in their general well-being and libido. It has also been suggested that these patients, left untreated, may suffer from the adverse effects of estrogen deficiency and therefore deserve to have their gonadal function restored to prevent development of premature osteoporosis. The data are suggestive but do not prove that these patients have an increased incidence of thinning of the bones.

The prolactinoma story is still evolving. Perhaps in another ten years we will have answers to the perplexing questions that give rise to the controversies of the management of this important condition.

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REFERENCES

1. Faglia G, Moriondo P, Beck-Peccoz P, et al: Use of neuroactive drugs and hypothalamic regulatory hormones in the diagnosis of hyperprolactinemic states, *In* Müller E (Ed): Neuroactive Drugs in Endocrinology, Vol 9. Amsterdam, Elsevier, 1980, pp 263-278

2. Franks S, Nabarro JDN, Jacobs HS: Prevalence and presentation of hyperprolactinemia in patients with 'functionless' pituitary tumors. Lancet 1977; 1:778-780

3. Costello RT: Subclinical adenoma of the pituitary gland. Am J Pathol 1936; 12:205-215

4. Burrow GN, Wortzman G, Rewcastle NB, et al: Microadenomas of the pituitary and abnormal sellar tomograms in an unselected autopsy series. N Engl J Med 1981 Jan 15; 304:156-158

5. Hardy J: Le prolactinome: Prolactinoma. Neurochirurgie 1981; 27 (suppl 1):1-110

6. Chiodini P, Liuzzi A, Cozzi R, et al: Size reduction of macroprolactinomas by bromocriptine or lisuride treatment. J Clin Endocrinol Metab 1981 Oct; 53:737-743

7. Serri O, Rasio E, Beauregard H, et al: Recurrence of hyperprolactinemia after selective transsphenoidal adenomectomy in women with prolactinoma. N Engl J Med 1983 Aug 4; 309:280-283

8. Thorner MO, Martin WH, Rogol AD, et al: Rapid regression of pituitary prolactinoma during bromocriptine treatment. J Clin Endocrinol Metab 1980; 51:438-445

9. Thorner MO, Perryman RL, Rogol AD, et al: Rapid changes of prolactinoma volume after withdrawal and reinstitution of bromocriptine. J Clin Endocrinol Metab 1981; 53:480-483

10. Tindall G, Kovacs K, Horvath E, et al: Human prolactin-producing adenomas and bromocriptine—A histological, immunocytochemical, ultrastructural, and morphometric study. J Clin Endocrinol Metab 1982; 55:1178-1183

Surgical Treatment for Congenital Heart Disease—Is It Corrective?

IN THE FOUR DECADES since surgical repair of congenital heart disease became common practice, the ingenuity of cardiovascular surgeons and pediatric cardiologists has made most lesions amenable to some form of surgical procedure. It has been acknowledged that some of these procedures are palliative, but the term "corrective surgery" has been applied increasingly, with the implication that closure of a defect or relief of an obstruction will return a patient to normal function. Unquestionably, most patients show relief of symptoms and improvement of exercise tolerance after an operation, but what is their long-term outlook?

Dr Perloff and his colleagues address this question in this issue, using a common lesion, tetralogy of Fallot, as a basis for discussion of problems that may be encountered after surgical "correction" of congenital cardiac lesions. It is recognized that following a surgical procedure, there may be residual lesions that are not evident clinically—such as small defects due to incomplete closure, or minor to moderate degrees of obstruction—and that serious complications such as complete heart block may result. However, there is an increasing realization that more subtle changes, which may have existed before or may present following the surgical procedure, could seriously interfere with patients' well-being and influence life expectancy. Also, persons with certain conditions have a high incidence of associated lesions that may not be diagnosed by routine physical examination, but that require continuing surveillance. Thus it is well known that up to 85% of patients with aortic coarctation have a bicuspid aortic valve,[1] which makes them susceptible to infective endocarditis.

Cardiac arrhythmias are not infrequent after an intracardiac operation; ventricular conduction disturbances and ventricular arrhythmias are common after repair of ventricular septal defects, tetralogy of Fallot and more complicated intraventricular anomalies, whereas surgical repair for atrial septal defects or insertion of an atrial baffle for aortopulmonary transposition predisposes to supraventricular tachycardia or sinus node dysfunction. Sudden death, which may occur months or even years after a surgical procedure for tetralogy of Fallot, has been associated with persisting ventricular premature contractions postoperatively. Garson and co-workers have related this to incomplete relief of right ventricular outflow obstruction, with elevation of right ventricular pressure above 60 mm of mercury.[2] Certainly the frequency of postoperative atrial arrhythmias has varied greatly in different centers and surgical technique appears to play an important role in the incidence; increasing appreciation of cardiac electrophysiology with appropriate modifications of technique may greatly reduce the frequency of this sequela.

Ventricular function following repair of congenital heart lesions has become a subject of increasing interest and concern.[3] It is not too surprising that after an incision into the right ventricle to approach a ventricular septal defect or relieve infundibular stenosis in tetralogy of Fallot, some interference with right ventricular function may occur. However, right ventricular function has been reported to be impaired in some adults following closure of atrial septal defects.[4] The mechanisms respon-